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Synthesis, Characterization and Antimicrobial Evaluation of Transition Metal(II) Complexes with Isatinimine Schiff bases and 8-Hydroxyquinoline

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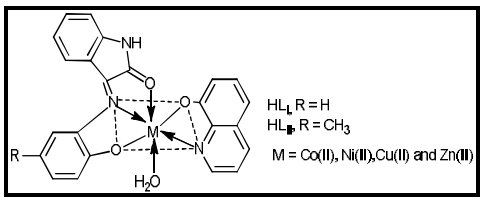
ABSTRACT

Cobalt(II), nickel(II), copper(II) and zinc(II) complexes of Isatinimine Schiff base ligands (HL_I-HL_{II}) derived from isatin with 2-aminophenol (HL_I), 2-amino-4-methyl phenol (HL_{II}) and heterocyclic nitrogen base 8-hydroxyquinoline (HQ) have been synthesized. The structure of all the compounds has been discussed on the basis of elemental analysis, molar conductance and spectroscopic techniques (IR, NMR and mass). Isatinimine Schiff base ligands existed as monobasic tridentate ONO bonded to metal ion through carbonyl oxygen, azomethine nitrogen and deprotonated enolic oxygen, whereas ligand HQ existed as monobasic bidentate ON coordinating through oxygen of hydroxyl group and nitrogen of quinoline ring. $M(L_{I-II})(Q).H_2O$ complexes were found to be non-electrolytic and monomeric in nature with octahedral or distorted octahedral geometries about metal centers. Agar plate disc diffusion method has been used for bio efficacy of compounds against various pathogenic Gram- positive bacteria viz. Bacillus subtilis, Micrococcus luteus, Gram negative bacteria viz. Pseudomonas aeruginosa, Pseudomonas mendocina and fungi Verticillium dahlia, Cladosporium herbarium, Trichophyton soudanense using different concentration (25, 50, 100, 200 μgmL^{-1}) of ligands and their complexes. Comparative study of zone of inhibition of Schiff base ligands, heterocyclic nitrogen base and their mixed ligand complexes indicated that complexes exhibit higher antimicrobial activity than the corresponding free ligands due to chelation process which reduces the polarity of metal ions.

Graphical Abstract



Transition metal complexes

Highlights

- Synthesis and characterization of mixed ligand tertradentate transition metal complexes.
- Evaluation for antibacterial and antifungal activity against gram positive bacteria *viz. Bacillus subtilis, Micrococcus luteus,* Gram negative bacteria *viz. Pseudomonas aeruginosa, Pseudomonas*

mendocina and fungi *Verticillum dahliae, Cladosporium herbarium, Trichophyton soudanense.*

- Transition metal complexes were found more active than the ligands

Keywords: Schiff base, Mononuclear, Bidentate, Pathogenic, Antimicrobial activity.

INTRODUCTION

The research in biochemical and medicinal chemistry is to find new compounds with plenty of biological activity and low cytotoxicity due to universal increase in the rate of microbial resistance to various antibiotics, leading to reduction in the efficiency of treatments [**1-3**]. Metal ion chelation therapy has attracted much attention in this field. Schiff base complexes with various metals has developed the new era in the coordination chemistry possessing remarkable applications in biological fields in agriculture as pesticides weedicides, industrial domain as catalysts, photoluminescence material, radical scavenging activity [**4, 5**]. A lot of work has been done on Schiff bases as they have different coordination modes, allowing for the synthesis of homo-and heterocomplexes.

In the present article, mixed ligand transition metal complexes are synthesized with different pharmacophores, which may lead to compounds with increasing biological profiles due to diverse functional groups that interact with biological receptors. Schiff bases derived from Isatinimine exhibit many neuropharmacological and neurophysiological effects like antimicrobial, antiviral, anticancer, anticonvulsant, antimalarial, anti-HIV, antiprotozoal, anthelminthic [**6-9**], and anti-inflammatory activities [**10-15**]. They are used in the storage as well as for transport of active material through membrane [**16**]. They display good DNA cleavage and binding activity which depend on the nature of metal atom, its coordination number, nature of alkyl group bound to metalatom and type of ligand attached. The interesting biological profile encourage us to synthesis and characterized transition metal(II) complexes using Isatinimine Schiff base ligands (HL_{I-II}) as primary ligand and 8-hydroxyquinoline (HQ) as secondary ligand and evaluated of their *in vitro* antimicrobial activity.

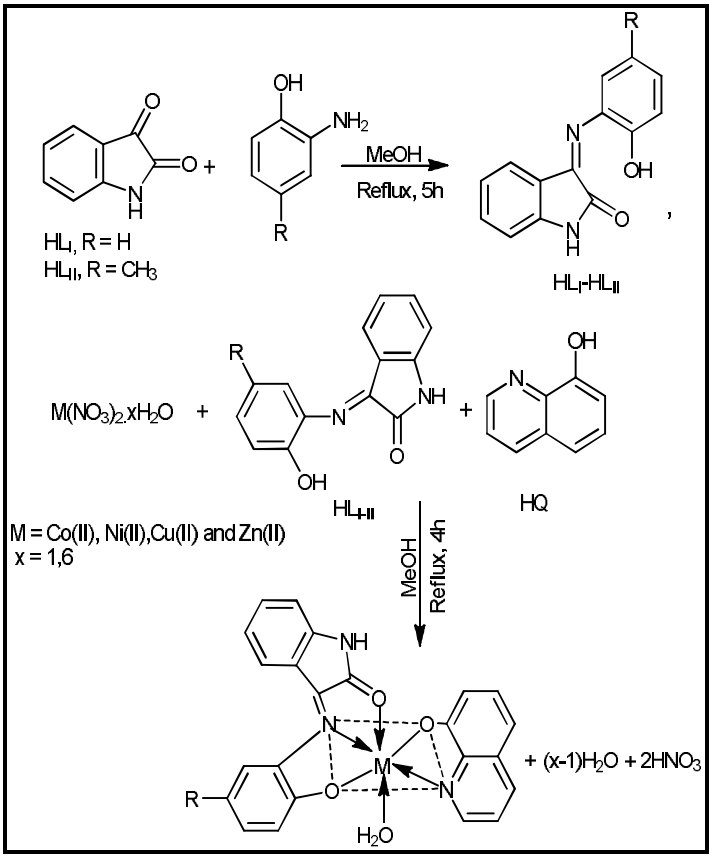
MATERIALS AND METHODS

All the chemicals were of analytical grade obtained from Aldrich and used as such without any further purification. Elemental C, H and N analysisof samples were carried out by using Perkin Elmer 2400 instrument. Metal contents were determined by using standard gravimetric methods: cobalt as cobalt pyridine thiocyanate, nickel as nickel dimethylglyoximate, copper as cuprous thiocyanate and zinc as zinc ammonium phosphate. IR spectra of Schiff bases and metal complexes were recorded on Shimadzu IR affinity-I 8000 FT-IR spectrometer using KBr disc. ^{1}H NMR and ^{13}C NMR were recorded on Bruker Avance II 300 MHz NMR spectrometer and all chemical shifts were reported in parts per million relativeto TMS as internal standard in $CDCl_3$. Mass spectra were recorded on a API 2000 (Applied Biosystems) mass spectrometer equipped with an electro spray source and a Shimadzu Prominence LC. Molar conductance measurement of $1x10^{-3}$ M solution in dry DMF at room temperature was carried out using a model-306-systronics conductivity bridge having cell constant equal to one.

General Procedure for the synthesis of transition metal complexes

Isatinimine Schiff base ligands: Schiff base ligands were synthesized by refluxing the reaction mixture of 2-aminophenol/substituted 2-aminophenol (10 mmol) with isatin (10 mmol) in methanolic solution by adding few drops of acetic acid in 1:1 molar ratio. The excess of solvent was evaporated and solid product was filtered, washed with methanol, recrystallized from methanol and dried under vacuum (Scheme 1).

Mixed ligand transition metal(II) complexes: Hydrated metal salt, $M(NO_3)_2.XH_2O$ (1mmol), methanolic solution of Schiff base Isatinimine ligands (HL_{I-II}) (1 mmol) was added to methanolic solution of 8-hydroxyquinoline (HQ) (1 mmol) with constant stirring in 1:1:1 molar ratio. Sodium hydroxide was added to maintain pH of solution. Solid complex obtained was filtered and washed with methanol to remove unreacted metal nitrates or ligands and dried under vacuum to obtained TLC pure product (Scheme I).



Scheme 1. Synthesis of Schiff base and their transition metal complexes.

RESULTS AND DISCUSSION

transition metal salts $M(NO_3)_2.xH_2O$ [M = Co(II), Ni(II), Cu(II) and Zn(II), x = 1,6] with tridentate Isatinimine Schiff base ligands- 3-(2-Hydroxy-phenylimino)-1,3-dihydro-indol-2-one (HL_I), 3-(2-Hydroxy-5-methyl-phenylimino)-1,3-dihydro-indol-2-one (HL_{II}) and bidentate heterocyclic nitrogen base 8-hydroxyquinoline (HQ). The compounds were air and moisture stable.

Physical and spectral data: The complexes were obtained as solids, insoluble in most organic solvents except DMF and DMSO. The low molar conductance values for the complexes in the range of 3.6-11.3 Ω^{-1} cm^2 mol^{-1} in dry DMSO indicated the non-electrolytic nature of complexes (Table 1). The spectral data and elemental analysis of the compounds were in good agreement with their structure, indicating the high purity of all the compounds. The analytical data indicated a 1:1:1 metal ligand stoichiometry.

IR spectra: For knowing binding modes of Schiff base ligands and their transition metal ions, IR spectra of compounds were recorded. On comparison of spectra, shifting of strong band at 1665 and 1670 cm^{-1} due to υ (C=N) azomethine group of Schiff base ligands to lower value of 1620-1642 cm^{-1}

Table 1. Physical and analytical data of transition metal(II) complexes of mixed ligand

S.No	Compounds	Mol. Formula of complex (mol.wt.)	Yield (%)	M.pt (°C)	Color	Found (calcd) (%)				Mass m/z	(Ω_M) x10^{-3}
						C	H	N	M		
1	HL_I	$C_{14}H_{10}N_2O_2$ (238.24)	75	180	Orange	70.19 (70.58)	4.76 (4.23)	11.35 (11.76)	238.6	--	--
2	HL_{II}	$C_{15}H_{12}N_2O_2$ (252.27)	78	164	Yellow	71.68 (71.42)	4.93 (4.79)	11.43 (11.10)	253.0	--	--
3	$Co(L_I)(Q).H_2O$	$C_{23}H_{17}N_3O_4Co$ (458.33)	75	> 295[d]	green	60.04 (60.27)	3.31 (3.74)	9.43 (9.17)	12.54 (12.86)	458.9	4.7
4	$Ni(L_I)(Q).H_2O$	$C_{23}H_{17}N_3O_4Ni$ (458.09)	77	> 290[d]	brown red	60.65 (60.30)	3.40 (3.74)	9.54 (9.17)	12.56 (12.81)	457.6	3.6
5	$Cu(L_I)(Q).H_2O$	$C_{23}H_{17}N_3O_4Cu$ (462.94)	78	> 285[d]	green	59.43 (59.67)	4.04 (3.70)	9.51 (9.08)	13.97 (13.73)	462.4	4.7
6	$Zn(L_I)(Q).H_2O$	$C_{23}H_{17}N_3O_4Zn$ (464.79)	70	> 290[d]	color-less	59.87 (59.43)	3.83 (3.69)	9.45 (9.04)	14.46 (14.07)	464.1	8.3
7	$Co(L_{II})(Q).H_2O$	$C_{24}H_{19}N_3O_4Co$ (472.36)	76	> 284[d]	green	61.43 (61.02)	4.35 (4.05)	8.54 (8.90)	12.63 (12.48)	472.9	9.4
8	$Ni(L_{II})(Q).H_2O$	$C_{24}H_{19}N_3O_4Ni$ (472.12)	78	> 285[d]	brown red	61.45 (61.06)	4.37 (4.06)	8.63 (8.90)	12.67 (12.43)	472.9	8.6
9	$Cu(L_{II})(Q).H_2O$	$C_{24}H_{19}N_3O_4Cu$ (476.97)	73	> 290[d]	green	60.02 (60.43)	4.36 (4.02)	8.63 (8.81)	13.56 (13.32)	476.2	6.8
10	$Zn(L_{II})(Q).H_2O$	$C_{24}H_{19}N_3O_4Zn$ (478.82)	75	> 280[d]	color-less	60.45 (60.20)	4.30 (4.00)	8.54 (8.78)	13.98 (13.66)	479.6	4.5

showed the participation of azomethine nitrogen in coordination[17]. Shift was also observed for υ (C=O) of isatin moiety towards lower value from 1710-1715 cm^{-1} to 1680-1685 cm^{-1}, indicated that carbonyl oxygen atom of isatin was one of the coordinating sites (Table 2). Further confirmation for coordination was observed by disappearance of OH band which was observed in ligand at 3250-3280 cm^{-1}. Coordination of 8-hydroxyquinoline was confirmed by absence of band at 3420 cm^{-1} due to υ (O-H) stretching vibration and band of υ (C=N) stretching vibration at 1575 cm^{-1} of quinoline ring was shifted to lower value, showed coordination of HQ with hydroxyl oxygen and nitrogen of quinoline ring. New stretching vibration was also observed at 534-550 cm^{-1} and 470-510 cm^{-1} which may be due to υ (M-N) and υ (M-O) vibrations [18]. Coordinated water molecule in the complexes was confirmed by the appearance of band between 3390-3440 cm^{-1} [19].

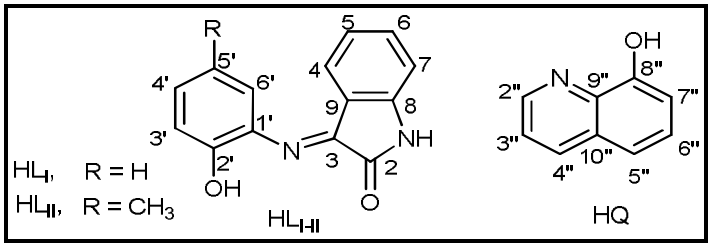
Table 2. Infrared spectral characteristics (υ, cm^{-1}) of Schiff base ligands and transition metal(II) complexes

Compounds	(N-H)	(C=O) Indole ring	(C=N)	(M-O)	(M-N)	(H-O-H)
HL_I	3193	1715	1670	--	--	--
HL_{II}	3192	1710	1665	--	--	--
$Co(L_I)(Q)H_2O$	3190	1682	1642	475	540	1560
$Ni(L_I)(Q)H_2O$	3195	1681	1630	483	547	1564
$Cu(L_I)(Q)H_2O$	3192	1685	1634	498	534	1558
$Zn(L_I)(Q)H_2O$	3190	1684	1638	485	545	1555
$Co(L_{II})(Q)H_2O$	3194	1682	1622	505	550	1568
$Ni(L_{II})(Q)H_2O$	3193	1683	1620	510	542	1563
$Cu(L_{II})(Q)H_2O$	3193	1680	1634	498	541	1564
$Zn(L_{II})(Q)H_2O$	3190	1683	1640	470	546	1570

^{1}H NMR and ^{13}C NMR spectra: The ^{1}H NMR and ^{13}C NMR spectra of Schiff base ligands (HL_{I-II}), HQ and their zinc(II) complexes are given in table-3. On comparison of ^{1}H NMR spectra of ligands and its zinc(II) complexes, the phenolic OH signal at δ 10.18-10.84 ppm of Isatinimine Schiff base ligands HL_{I-II} and at δ 12.92 ppm of HQ showed deprotonation of hydroxyl group when attached to zinc metal ion. Ligand (HL_{I-II}) showed a peak at δ 9.24-9.23 ppm due to -NH- proton and remains unaltered showing its non-participation in bond formation with metal atom. Aromatic protons were

observed in the range of δ 6.77-7.63 ppm for HL_{I-II} and δ 7.01-8.84 ppm for HQ ligand. With complexation, due to deshielding very small variation was observed in chemical shift of aromatic protons of isatin ring, quinoline ring and phenolic ring. The presence of water molecule in complexes was confirmed by the appearance of new signal around δ 3.50 due to coordinated H_2O proton. In ^{13}C NMR spectra of complexes, signals of azomethine carbon atom of Schiff base ligands HL_{I-II} was shifted from δ 164.72-164.84 to δ 165.87-165.97 ppm, carbonyl carbon of ligands from δ158.48-159.74 to δ 160.34-161.27ppm and carbon attached to hydroxyl of phenolic ring was shifted from δ 143.45-145.60 to δ 144.31–147.23 ppm suggested coordination of ligand with zinc metal atom. The signal of carbon attached to hydroxyl group of ligand HQwas shifted from δ 153.74 to δ 154.36-154.98 ppm, and shift in (C=N) carbon atom was observed from δ 150.30 to δ 152.18-152.40 and not much variation is observed in other aromatic carbon atom signals (Table 3).

Table 3. ^{1}H and ^{13}C NMR spectral characteristics (δ) of Isatinimine Schiff base ligands and transition metal (II) complexes



Ligands	^{1}H NMR($CDCl_3$) δ in ppm	^{13}CNMR($CDCl_3$) δ in ppm
HL_I	10.84 (s, 1H, OH), 9.23 (s, 1H, NH), 7.63 (d, 1H, C_4-H, , J = 8.34 Hz), 7.32 (t, 1H, C_5-H), 7.45 (t, 1H, C_6-H), 7.68 (d, 1H, C_7-H, J = 8.34 Hz), 7.49 (d, 1H, C_3'-H, J = 7.84 Hz,), 6.98 (t, 1H, C_4'-H), 7.24 (t, 1H, C_5'-H), 6.94 (d, 1H, C_6'-H, J = 8.81 Hz)	164.84 (C=N), 159.74 (C=O), 132.42 (C_4), 127.40 (C_5), 134.05 (C_6), 123.58 (C_7), 141.71 (C_8), 127.10 (C_9), 150.83 (C_1'), 143.45 (C_2'), 127.48 (C_3'), 125.43 (C_4'), 131.34 (C_5'), 120.40 (C_6')
HL_{II}	10.18 (s, 1H, OH), 9.24 (s, 1H, NH), 7.65 (d, 1H, C_4-H, J = 8.82 Hz), 7.35 (t, 1H, C_5-H), 7.42 (t, 1H, C_6-H), 7.67(d, 1H, C_7-H, J = 8.82 Hz), 7.03 (s, 1H, C_3'-H), 6.98 (d, 1H, C_5'-H, J = 7.62 Hz), 6.77 (d, 1H, C_6'-H, J = 7.62Hz)	164.72 (C=N), 158.48 (C=O), 132.20 (C_4), 127.24 (C_5), 134.05 (C_6), 123.55 (C_7), 141.74 (C_8), 127.15 (C_9), 150.84 (C_1'), 143.64 (C_2'), 127.14 (C_3'), 134.62 (C_4'), 132.15 (C_5'), 119.80 (C_6')
HQ	12.92 (s, 1H, OH), 8.84 (d, 1H, C_2''-H, J = 9.02 Hz), 7.28 (t, 1H, C_3''-H), 7.99 (d, 1H, C_4''-H, J = 8.04 Hz), 7.36 (d, 1H, C_5''-H, J = 8.28 Hz), 7.28 (t, 1H, C_6''- H), 7.01 (d, 1H, C_7''-H, J = 9.18 Hz)	150.30 (C_2''), 125.64 (C_3''), 137.40 (C_4''), 120.42 (C_5''), 128.92 (C_6''), 116.40 (C_7''), 153.74 (C_8''), 138.81 (C_9''), 130.52 (C_{10}'')
Zn(LI)(Q)H_2O	9.23 (s, 1H, NH), 7.64 (d, 1H, C4-H, J = 6.08 Hz), 7.32 (t, 1H, C5-H), 7.47 (t, 1H, C6-H), 7.68 (d, 1H, C7-H, J= 4.14 Hz), 7.51 (d, 1H, C3′-H, J = 9.04 Hz,), 6.96 (t, 1H, C4′-H), 7.24 (t, 1H, C5′-H), 6.99 (d, 1H, C6′-H, J = 6.18 Hz), 8.89 (d, 1H, C2″-H, J= 8.04 Hz), 7.28 (t, 1H, C3″-H), 8.01 (d, 1H, C4″-H, J = 3.18 Hz), 7.36 (d, 1H, C5″-H, J = 9.04 Hz), 7.29 (t, 1H, C6″- H), 7.04 (d, 1H, C7″ -H, J = 6.36 Hz), 3.50 (s, 2H, H2O)	165.96 (C=N), 160.34 (C=O), 132.84 (C4), 127.52 (C5), 134.41 (C6), 123.94 (C7), 141.52 (C8), 126.92 (C9), 151.87 (C1′), 145.93 (C2′), 129.02 (C3′), 125.84 (C4′), 131.04 (C5′), 122.23 (C6′), 152.20 (C2″), 125.98 (C3″), 137.40 (C4″), 120.42 (C5″), 128.92 (C6″), 118.01 (C7″), 154.63 (C8″), 139.04 (C9″), 131.04 (C10″)
Zn(LII)(Q)H_2O	9.25 (s, 1H, NH), 7.65 (d, 1H, C4-H, J= 7.04 Hz), 7.35 (t, 1H, C5-H), 7.42 (t, 1H, C6-H), 7.68 (d, 1H, C7-H, J = 9.04 Hz), 7.06 (s, 1H, C3′-H), 6.99 (d, 1H, C5′-H, J = 8.14 Hz), 6.92 (d, 1H, C6′-H, J = 7.62 Hz), 8.92 (d, 1H, C2″-H, J = 4.36 Hz), 7.29 (t, 1H, C3″-H), 7.96 (d, 1H, C4″-H, J = 6.08 Hz), 7.38 (d, 1H, C5″-H, J = 9.04 Hz), 7.28 (t, 1H, C6″- H), 7.08 (d, 1H, C7″-H, J = 6.48 Hz), 3.51 (s, 2H, H2O)	165.87 (C=N), 161.27 (C=O), 131.84 (C4), 128.01 (C5), 134.05 (C6), 123.82 (C7), 141.93 (C8), 127.80 (C9), 151.04(C1′), 144.31 (C2′), 129.18 (C3′), 134.84 (C4′), 131.89 (C5′), 120.04 (C6′), 152.18 (C2″), 126.18 (C3″), 137.98 (C4″), 120.98 (C5″), 129.04 (C6″), 118.02 (C7″), 154.36 (C8″), 138.04 (C9″), 131.89 (C10″)

Mass spectra: The LC-mass spectra of ligands and their transition metal(II) complexes were recorded and were in close agreement with molecular weight of compounds (Table 1). The mass spectra of HL_{II} ($C_{15}H_{12}N_3O_2$) showed molecular ion peak at m/z 253.0 and its corresponding cobalt complex $Zn(L_{II})(Q).H_2O$ ($C_{24}H_{19}N_3O_4Zn$) showed molecular ion peak at m/z 478.4 which was in accordance with molecular weight of compounds.

Biological activity

Tested microorganisms: Microorganisms used for antibacterial and antifungal activity were:Gram positive bacteria- *Bacillus subtilis* (MTCC No. 1790), *Micrococcus luteus* (MTCC No. 4821), Gram negative bacteria- *Pseudomonas aeruginosa* (MTCC No. 9126), *Pseudomonas mendocina* (MTCC No. 7094) and fungi *Verticillium dahlia* (MTCC No. 2063), *Cladosporium herbarium* (MTCC No. 351), *Trichophyton soudanense* (MTCC No.7859). The bacteria and fungi were sub cultured on Nutrient agar and Sabouraud dextrose agar respectively. The experimental values were compared with standard drugs *Streptomycin* for antibacterial activity and *Fluconazole* for antifungal activity.

Antibacterial activity assay: Antibacterial activity of samples (1-11) was determined by using agar well diffusion method showing the zone of inhibition. Stock solution was prepared by dissolving compound in minimum amount of DMSO. Nutrient agar (15 mL) for activation was prepared for tested target microorganism cultures. Micropipette with sterilized tips was used for inoculation, activated strain (100 µL) was placed onto surface of agar plate, spread with the help of spreader over the whole surface and two wells of 10 mm diameter were dug in media. Sterilized stock solutions were used for the application in the well of inoculated agar plates. In this well of inoculated agar plates 100 µL of solution was poured and incubated at 37°C for 48 h.

Antifungal activity assay: For *in vitro* antifungal activity the molds were grown on sabouraud dextrose agar (SDA) at 25°C for 7 days. 15 mL of molten SDA (45°C) was added to 100 µL volume of each compound having concentration of 100 µg mL^{-1}, reconstituted in the DMSO, poured into a sterile Petri plate and allowed to solidify at room temperature. The solidified poisoned agar plates were inoculated at the centre with fungal plugs (10 mm) obtained from actively growing colony and incubated at 25°C for 7 days. Diameter of the fungal colonies was measured and expressed as percent mycelial inhibition:

$$\text{Inhibition of mycelial growth \%} = (d_c - d_t)/d_c \times 100$$

Where, *dc* is average diameter of fungal colony in negative control, d_t average diameter of fungal colony in experimental plates.

Antimicrobial activity: The antimicrobial activity of Isatinimine Schiff base ligands $HL_{I\text{-}II}$, 8-hydroxyquinoline (HQ) and their mixed ligand transition metal (II) complexes **[**$M(L_{I\text{-}II})(Q)H_2O$)] were tested against Gram positive bacteria (*Bacillus subtilis, Micrococcus luteus*), Gram negative bacteria (*Pseudomonas aeruginosa, Pseudomonas mendocina)* and fungi (*Verticilliumdahlia, Cladosporium herbarium, Trichophyton soudanense)*using agar plate diffusion method at different concentration in DMSO. Positive Controls (standards drugs Streptomycin and Fluconazole) produced significantly sized inhibition zones against the tested microbial strains and negative control (DMSO) produced no observable inhibitory effect against any of the tested organism. The zone of inhibition and mycelial growth inhibition against the growth of microorganisms for the compounds are summarized in (Table-4,5) and graphical representations of average activity were given in figure 1 and 2.

The pharmacological data showed that the synthesized compounds were found to be highly potent against fungal strains as compared to bacterial strains. Ligands $HL_{(I\text{-}II)}$ and HQ were found to be less active than their respective transition metal(II) complexes and showed zone of inhibition for antibacterial activity in range of 8-16 mm, with complexation it increased in range of 11-25 mm. All

Table 4. The *in vitro* antibacterial activity of Schiff base ligands and their transition metal(II) complexes

S. No	Compounds	Zone of Inhibition(mm)															
		Gram +ve								Gram –ve							
		B. subtilis				*M. Luteus*				*P.aeruginosa*				*P. mendocina*			
		25	50	100	200	25	50	100	200	25	50	100	200	25	50	100	200
1	HL_I	8	8	10	11	8	9	10	12	9	9	11	12	8	10	10	12
2	HL_{II}	8	9	10	12	10	10	12	14	9	10	11	12	9	11	12	13
3	HQ	8	8	10	11	9	10	10	11	8	9	10	10	8	10	10	11
4	$Co(L_I)(Q)H_2O$	13	14	16	16	11	12	14	15	11	11	14	15	11	12	14	16
5	$Ni(L_I)(Q)H_2O$	14	16	16	17	12	12	14	17	12	14	14	16	12	12	14	16
6	$Cu(L_I)(Q)H_2O$	15	16	17	20	13	14	15	17	14	16	17	19	14	17	18	21
7	$Zn(L_I)(Q)H_2O$	11	13	13	15	8	10	12	13	9	12	13	14	10	12	14	15
8	$Co(L_{II})(Q)H_2O$	12	15	15	17	10	12	12	15	12	14	14	17	13	15	16	17
9	$Ni(L_{II})(Q)H_2O$	13	16	17	18	12	15	15	17	13	15	15	17	14	16	16	18
10	$Cu(L_{II})(Q)H_2O$	14	15	18	20	14	15	16	19	15	16	18	21	15	18	18	21
11	$Zn(L_{II})(Q)H_2O$	10	11	12	14	10	13	13	14	11	12	14	16	12	12	15	19
12	*Streptomycin*	19	21	25	26	19	20	23	25	20	23	25	28	22	25	27	30

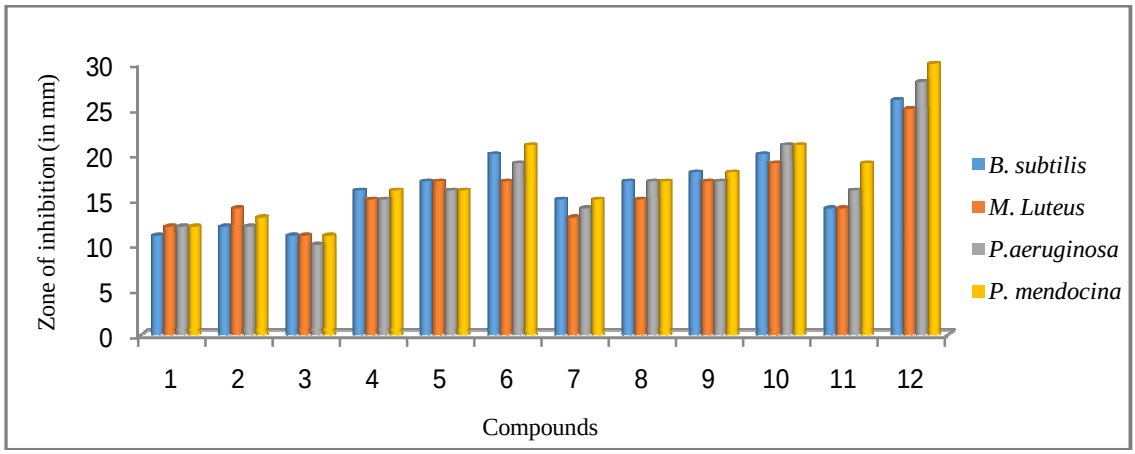


Figure 1. Graphical representation of *in vitro* antibacterial activity of Schiff base ligands and their transition metal(II) complexes.

the ligands showed mycelial growth inhibition in the range of 42.3-52.8% and it increased in the range of 50.2-63.4 % in case of complexes. Among Schiff bases, the order of reactivity of ligands were HL_{II}> HL_I> HQ. Ligand with halo group is more active than the methyl group.

Among all the complexes Cu(II) and Ni(II) complexes were greatly active against bacterial and fungal strains. Zone of inhibition against all strains follows the order: Cu(II) > Ni(II) > Co(II) >Zn(II) > HL_{I-II} > HQ. The higher activity of metal complexes may be due to the effect of metal ions on the normal cell membrane [**20-22**]. The variation in the biological activity of complexes against different microorganism depends either on the impermeability of cells of the microbes or ribosomal differences of microbes.

The enrichment observed in biological activity on complexation is explained on basis of chelation theory [**23**]. According to this theory, the normal cell process may be affected by the formation of hydrogen bond through the donor atoms with the active centers of cell constituents. Metal chelates display both polar and non-polar properties which make them suitable for permeation into cells and tissues. The polarity of metal ion gets reduced due to overlap of ligand orbitals when chelated, chelation increases the delocalization of pi-electrons over the entire chelate ring and enhance the penetration of the complexes into lipid membranes. It increases the hydrophilic and lipophilic nature of the central metal ions, leading to liposolubility and permeability through the lipid layer of cell membranes.

Table 5. The *in vitro* antifungal activity of Schiff base ligands and their transition metal(II) complexes

S. No	Compounds	Mycelial growth Inhibition (%)											
		V. dahlia				*C.herbarium*				*T. soudanense*			
		25	50	100	200	25	50	100	200	25	50	100	200
1	HL_I	44.7	46.3	47.4	48.9	43.2	45.3	47.4	48.2	44.5	44.9	45.8	47.4
2	HL_{II}	46.5	48.9	49.2	49.9	45.1	47.4	48.3	49.4	45.2	46.8	46.9	48.3
3	HQ	42.3	44.8	46.4	48.9	42.3	44.1	45.2	46.8	41.2	41.9	42.3	43.7
4	$Co(L_I)(Q)H_2O$	50.8	52.4	53.7	55.4	53.7	56.5	57.4	59.4	50.2	52.3	52.8	54.7
5	$Ni(L_I)(Q)H_2O$	52.4	53.7	54.8	56.4	52.4	53.7	54.5	57.3	50.8	52.4	52.9	53.9
6	$Cu(L_I)(Q)H_2O$	54.2	56.3	56.9	58.4	53.9	56.8	58.1	59.9	53.2	54.3	55.4	56.8
7	$Zn(L_I)(Q)H_2O$	50.7	52.6	54.2	54.9	50.8	52.4	53.8	55.4	51.2	51.9	53.4	54.3
8	$Co(L_{II})(Q)H_2O$	54.3	56.2	56.8	57.4	53.2	54.5	54.9	55.2	54.2	55.6	56.4	57.1
9	$Ni(L_{II})(Q)H_2O$	54.1	54.4	55.7	56.4	52.8	53.4	53.9	55.4	53.8	54.3	55.4	56.7
10	$Cu(L_{II})(Q)H_2O$	56.4	57.3	58.4	59.8	55.3	57.0	58.2	59.9	55.4	56.7	56.9	58.2
11	$Zn(L_{II})(Q)H_2O$	53.2	54.3	55.6	56.4	52.3	54.6	55.8	57.4	52.8	53.2	53.6	54.7
12	*Fluconazole*	76.2	79.4	79.8	81.2	75.8	77.2	78.3	81.9	74.1	76.4	79.6	83.3

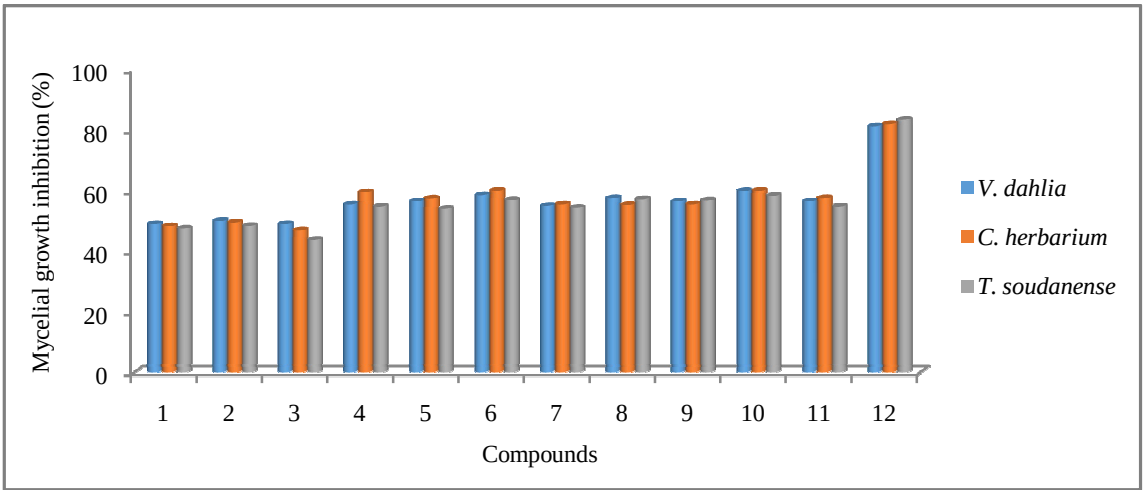


Figure 2. Graphical representation of *in vitro* antifungal activity of Schiff base ligands and their transition metal(II) complexes.

Copper Complex with 59.9% mycelia growth and was found to be most effective antimicrobial agent in the whole series and can be used in pharmaceutical industry for mankind after testing its toxicity to human beings.

APPLICATION

The synthesized compounds exhibited lot of applications in biological field and when we compared the result of synthesized compounds with the standard drugs it was found that some synthesized compounds were more active than the standard. So, these compounds were better used as antimicrobial drug and have pharmaceutical application.

CONCLUSION

Based on the various observations of spectroscopic techniques (IR, NMR and mass) it revealed that Schiff base ligands HL_{I-II} existed as monobasic tridentate ONO bonded to metal ion through carbonyl oxygen, azomethine nitrogen, deprotonated enolic oxygen and HQ ligand existed as monobasic bidentate ON bonded through oxygen of hydroxyl group and nitrogen of quinoline ring. Mononuclear structure with octahedral or distorted octahedral geometry has been proposed for complexes. The

antimicrobial activities against various bacterial and fungal strains showed that the metal complexes exhibited enhanced activity in comparison to their respective Schiff bases under identical experimental conditions on complexation. Further, it was found that compounds with halo groupshowed good to excellent potency against bacterial and fungal strains. The order for antimicrobial activity was found to be Cu(II) > Ni(II) > Co(II) >Zn(II) > $HL_{I\text{-}II}$ > HQ ligands against all the species of tested microorganisms. Compounds **10, 6** were most potent antimicrobial agents as they possess most prominent and reliable activity.

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